

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference EX04-057C-PC	<b>FOR FURTHER ACTION</b>	See item 4 below
International application No. PCT/US2004/026338	International filing date ( <i>day/month/year</i> ) 12 August 2004 (12.08.2004)	Priority date ( <i>day/month/year</i> ) 14 August 2003 (14.08.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant EXELIXIS, INC.		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- |                                     |              |   |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I    | Basis of the report   |
| <input type="checkbox"/>            | Box No. II   | Priority  |
| <input type="checkbox"/>            | Box No. III  | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability  |
| <input type="checkbox"/>            | Box No. IV   | Lack of unity of invention  |
| <input checked="" type="checkbox"/> | Box No. V    | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input type="checkbox"/>            | Box No. VI   | Certain documents cited   |
| <input type="checkbox"/>            | Box No. VII  | Certain defects in the international application  |
| <input type="checkbox"/>            | Box No. VIII | Certain observations on the international application   |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No. +41 22 740 14 35	Date of issuance of this report 07 June 2006 (07.06.2006)  Authorized officer  <div style="text-align: center; font-weight: bold; font-size: 1.2em;">Nora Lindner</div>  Telephone No. +41 22 338 89 65
---	--

# PATENT COOPERATION TREATY

REC'D 12 MAY 2006

WIPO

PCT

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:  
LALEH SHAYESTEH  
170 HARBOR WAY  
P.O. BOX 511  
SOUTH SAN FRANCISCO, CA 94083-0511

## PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Applicant's or agent's file reference <b>EX04-057C-PC</b>		Date of mailing (day/month/year) <b>10 MAY 2006</b> <b>FOR FURTHER ACTION</b> See paragraph 2 below
International application No. <b>PCT/US04/26338</b>	International filing date (day/month/year) <b>12 August 2004 (12.08.2004)</b>	Priority date (day/month/year) <b>14 August 2003 (14.08.2003)</b>
International Patent Classification (IPC) or both national classification and IPC <b>IPC(7): C07K 16/40; C12Q 1/00 and US Cl.: 435/4, 7.23,</b>		
Applicant <b>ELELIXIS</b>		

1. This opinion contains indications relating to the following items:

- ☒ Box No. I      Basis of the opinion
- ☐ Box No. II      Priority
- ☐ Box No. III      Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV      Lack of unity of invention
- ☒ Box No. V      Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI      Certain documents cited
- ☐ Box No. VII      Certain defects in the international application
- ☐ Box No. VIII      Certain observations on the international application

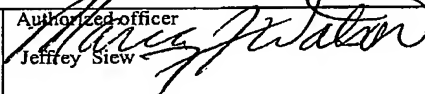
### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230	Date of completion of this opinion <b>26 September 2005 (26.09.2005)</b>	Authorized officer  Jeffrey Siew Telephone No. 571-272-1600
--	---	--

Form PCT/ISA/237 (cover sheet) (April 2005)

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US04/26338

Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of:

- ☒ the international application in the language in which it was filed  
☐ a translation of the international application into \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

- ☐ a sequence listing  
☐ table(s) related to the sequence listing

b. format of material

- ☐ on paper  
☐ in electronic form

c. time of filing/furnishing

- ☐ contained in the international application as filed.  
☐ filed together with the international application in electronic form.  
☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

International application No.  
PCT/US04/26338

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>NONE</u>	YES
	Claims <u>NONE</u>	NO
Inventive step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-25</u>	NO
Industrial applicability (IA)	Claims <u>NONE</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Claims 1-25 lack inventive under PCT Article 33(3) as being obvious over Bienz et al., (US Patent Application Publication, US2002/0015943) in view of Chen et al., (Lab Invest, vol 59, page 453, 1988) and Monga et al., (Gastroenterology, vol 124, page 202-16, Jan, 2003).

Bienz et al., teach a method of identifying a modulator in  $\beta$ -catenin pathway comprising an assay system of binding polypeptide of  $\beta$ -catenin, APC. Bienz et al., teach that the test compound to modulate binding may be determined by determine the binding of  $\beta$ -catenin polypeptide and APC polypeptide in the presence or absence of the test compound (para 11-17 and 45). Bienz et al., also teach the assay system in cell line comprising APC or  $\beta$  catenin truncation or mutation, which results in defective beta catenin function (para 38 and 103-104). Bienz et al., also teach that test compound could be antibody, peptide, nucleic acid, small molecule, which can be used in vitro cell system or administration to the individual (para 72).

Chen et al., a synthetic inhibitor of arylsulfase, Sodium 2-hydroxy-5- $\alpha$ -toluenesulfonated (HNT) inhibit specifically the growth of capillary blood vessels and potentiate antiangiogenic activity when the concentration of heparin was suboptimal.

Monga et al., teach a phosphorodiamidate morpholino ligomer (PMO) antisense to beta-catenin, which effectively inhibits synthesis of its protein and modulate cell proliferation and apoptosis for the cells (abstract).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to use the method of identifying a modulator in  $\beta$ -catenin pathway taught by Bienz et al., comprising arylsulfatase inhibitor of Chen et al.'s and PMO antisense of Monga et al.'s teachings. One of ordinary skill in the art would have been motivated with a reasonable expectation of success to apply the teachings of Chen et al., and Monga et al., to the teaching of Bienz et al., to use the method of identifying a modulator in  $\beta$ -catenin pathway because Bienz et al., have shown a method of identifying a modulator, Chen has shown HNT as a sulfatase inhibitor, which modulate the activity of sulfatase and Monga et al., have shown PMO antisense for-catenin.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/26338

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07K 16/40; C12Q 1/00

US CL : 435/4, 7.23,

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 435/4, 7.23,

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Bienz et al., US Patent Application Publication, US2002/0015943.	1-25
---		-----
Y	Chen et al., Lab Invest, vol 59, page 453, 1988	1-25
Y	Monga et al., Gastroenterology, vol 124, page 202-16, Jan, 2003	1-25

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

Special categories of cited documents:	
"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search

26 September 2005 (26.09.2005)

Name and mailing address of the ISA/US

Mail Stop PCT, Attn: ISA/US  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, Virginia 22313-1450

Facsimile No. (703) 305-3230

Date of mailing of the international search report

10 MAY 2006

Authorized officer

Jeffrey Siev

Telephone No. 571-272-1600